Cleveland Clinic Innovations

Auto-Antibody Driven Allosteric Modulation of β1AR Signaling

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PRODUCT
Antibody therapeutic

INDICATION
Heart failure, cardiovascular disease

VALUE PROPOSITION
Improved clinical outcomes for heart failure patients and those on β-blockers.

DEVELOPMENT STAGE
In vitro preclinical development

INTELLECTUAL PROPERTY
PCT/US2022/014951

RELATED PUBLICATIONS

Tang, W. H. W., et al. (2022). J Cardiovasc Pharmacol. 2022 Sep 1;80(3):354-363. PMID: 35323150

Mohan ML … **Tang WHW**, et al. Mol Biol Cell. 2021 Apr 1;32(7):622-633. PMID: 33534612

Nagatomo Y … **Tang WHW**, et al. J Am Coll Cardiol. 2017 Feb 28;69(8):968-977. PMID: 28231950

Nagatomo Y … **Tang WHH**. J Card Fail. 2016 Jun;22(6):417-22. PMID: 26997620

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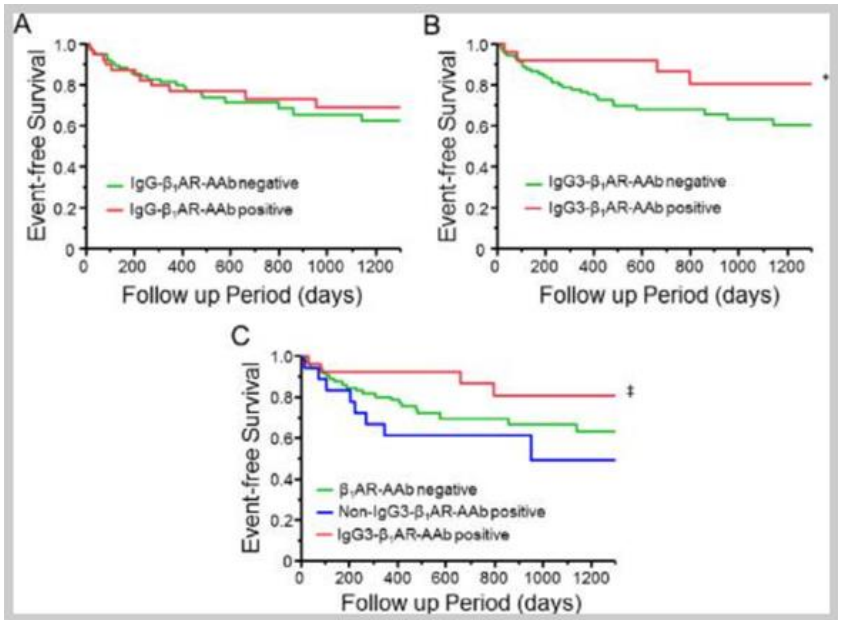
OPPORTUNITY

- Dysregulation of the immune system is considered to be one of the central players in cardiac pathogenesis.
- β-blockers, a primary therapy for cardiovascular disease, provide benefit by impeding Beta-1 adrenergic receptor (β1AR) signals.
- Autoantibodies against β1AR have been observed in up to 40% of patients with heart failure and recent onset dilated cardiomyopathy (DCM).
- Recent studies suggested that a subset of auto-antibodies identified in patients with DCM may be associated with better rather than worse clinical outcomes and myocardial recovery.

SOLUTION

- Cleveland Clinic researchers have identified a subtype of auto-antibodies that may generate allosteric modulation of β1AR signaling response.
- The sequencing and characterization of the autoantibody epitopes and facilitated identification of key allosteric binding sites that induce unique β1AR signaling patterns.
- These binding sites has led to the development of designer antibody and nanobody therapeutics for treating cardiovascular disease, specifically DCM.
- Lead candidate identification and optimization is ongoing.



Kaplan-Meier survival curves for the composite endpoint of all-cause death, cardiac transplantation, or hospitalization resulting from the exacerbation of heart failure